INFORMED CONSENT

TITLE OF RESEARCH: RTOG 0421 – A Phase III Trial for Locally Recurrent, Previously Irradiated Head and Neck Cancer: Concurrent Re-Irradiation and Chemotherapy Versus Chemotherapy Alone

SPONSOR: Radiation Therapy Oncology Group

INVESTIGATOR: Ruby F. Meredith, MD, PhD

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PURPOSE OF STUDY

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have head and neck cancer for which you have previously received radiation therapy and for which you cannot undergo surgery.

The purpose of this study is to compare the effects, good and/or bad, of re-irradiation and chemotherapy with chemotherapy alone on you and your head and neck cancer to find out which is better. In this study, you will receive either the re-irradiation and chemotherapy or chemotherapy alone.

About 240 people nationwide will take part in this study. We anticipate enrolling 14-21 at UAB.

Consent Form Approved 01-26-05
Expiration Date 07-20-06

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Participant's Initials: _________
EXPLANATION OF PROCEDURES

Before you begin the study, you will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- A physical exam
- An evaluation of your weight and of how many calories you are receiving each day
- Blood tests
- CT (Computed Tomography) scan of your chest; a CT scan is a study using x-rays to look at one part of your body
- CT scan or MRI (Magnetic Resonance Imaging) of your tumor; an MRI is imaging using a strong magnetic field to look at one part of your body
- CT scan of your abdominal area, if advised by your study doctor
- Biopsy of your tumor
- For women able to have children, a pregnancy test
- For participants receiving re-irradiation, a dental evaluation before receiving radiation
- A x-ray exam of the blood flow in the arteries in your neck, if advised by your study doctor
- If advised by your study doctor, an exam of the lining of your digestive tract; this involves putting a tube into your mouth and down your swallowing tube into the stomach and intestines to see the lining.
- An evaluation of your speech and/or swallowing, if advised by your study doctor

During the study, if the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

- A physical exam
- Blood tests

You will need these tests and procedures that are part of regular cancer care. They are being done more often because you are in this study.

For participants receiving chemotherapy alone,
Before each cycle of chemotherapy:
- A physical exam by your study doctor and by a Medical Oncologist
- Blood tests
Every 2 cycles of chemotherapy:
- A physical exam by your study doctor and by a Medical Oncologist
- Blood tests
- A CT scan or MRI of your tumor

You will need these tests and procedures in follow up visits. They are being done to see how you and your cancer was affected by the treatment you received.

At 3 months from start of treatment:
- For participants receiving re-irradiation, a CT scan or MRI of your tumor

Every 3 months for 2 years, every 6 months for 3 years, then annually:
- A physical exam by your study doctor and by a Medical Oncologist
- Blood tests
- A CT scan or MRI of your tumor, if advised by your study doctor
- A Chest CT scan, if advised by your study doctor
- A CT scan of your abdomen, if advised by your study doctor

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your study doctor can choose the group you will be in. You will have an equal chance of being placed in either group.

If you are in Group 1 (often called "Arm 1"), you will receive radiation therapy and chemotherapy every other week for 4 cycles (during weeks 1, 3, 5, and 7).

You will receive radiation therapy twice a day, Monday through Friday, every other week. Each radiation treatment will take about 5-10 minutes, and there will be at least 4 hours between the two daily treatments.

Between the radiation treatments each day, you will receive two chemotherapy drugs, paclitaxel and cisplatin, through your vein. Receiving the paclitaxel takes about one hour, and receiving the cisplatin takes about 30 minutes.

During weeks 2, 4, 6, and 8, you will not receive radiation or chemotherapy. Since chemotherapy drugs can decrease your white blood cells that fight infection, you will be given G-CSF, a drug to help your body make white blood cells. You will receive an injection of G-CSF under your skin once a day for 8 days, Saturday through Saturday, during each of the four weeks.

If you are in Group 2 (often called "Arm 2"), you will receive chemotherapy alone. Your study doctor and you will discuss the 3 types of chemotherapy available in this study and decide which chemotherapy is best for you. Each of the 3 treatments available includes a standard chemotherapy drug, cisplatin, which is given through your vein over about an hour. You also will receive fluids through your vein before and after each chemotherapy treatment.
Cisplatin will be given with one of the following drugs: 5-fluorouracil (also called 5-FU), paclitaxel, or docetaxel. If you receive 5-FU, it will be given through your vein over 4 days (96 hours) after the cisplatin, either as an inpatient or an outpatient. If you receive paclitaxel, it will be given through your vein over 3 hours, just prior to the cisplatin. If you receive docetaxel, it will be given through your vein over 1 hour, just prior to the cisplatin.

You will receive chemotherapy once every 3-4 weeks (1 cycle length), and your study doctor will examine you after every 2 cycles of chemotherapy. If your cancer is responding to the chemotherapy or remains stable (does not grow), then you will continue receiving chemotherapy for as long as it continues to help you (for at least 9 weeks and possibly for 18 weeks or longer).

If your cancer worsens, you and your study doctor will discuss other treatments, which can include re-irradiation with chemotherapy as given in Group 1 (as long as there are no new cancers in areas other than your current cancer).

Both groups: When you are finished having treatment, you will be seen in follow-up visits every 3 months for 2 years, every 6 months for 3 years, then yearly.

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**Study Plan**

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.

Randomize
(You will be in Group 1 or 2)

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**Group 1**
Re-Irradiation and Chemotherapy

Radiation Therapy 2x/day, 5x/week, every other week for about 8 weeks

Chemotherapy on weeks 1, 3, 5, and 7. G-CSF on weeks 2, 4, 6, and 8.

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**Group 2**
Chemotherapy

Chemotherapy once every 3-4 weeks, for at least 9 weeks and possibly for 18 weeks or longer (if your cancer doesn’t grow)
LENGTH OF STUDY
Group 1 participants will receive treatment for about 8 weeks. Group 2 participants will receive treatment for at least 9 weeks and possibly for 18 weeks or more, if there is no evidence of cancer growth.

After you are finished treatment, the study doctor will ask you to visit the office for follow-up exams for at least every 3 months for 2 years, every 6 months for 3 years, then yearly.

The doctor may decide to take you off this study if it is in your medical best interest, your condition worsens, or new information becomes available and this information suggests the treatment will be ineffective or unsafe for you. It is unlikely, but the study may be stopped due to lack of funding or participation.

You can stop participating at any time. However, if you decide to stop participating in the study, we ask you to talk to the study doctor and your regular doctor first.

RISKS AND DISCOMFORTS
You most likely will have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don’t know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects.

The combination of chemotherapy and radiation that some participants will receive in this study may result in more serious side effects or unexpected side effects than result in receiving either of these treatments alone. Many side effects go away soon after you stop receiving radiation and/or chemotherapy. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks Associated With Re-irradiation

Likely
- Sores in mouth or throat
- Temporary loss of taste
- Temporary skin redness or peeling in the treated area
- Dryness of the mouth
- Hoarseness
- Decrease in white blood cell count, which may increase the risk of infection, decreased healing, and/or bleeding
- Dental cavities
Less Likely, But Serious

- Severe irritation of the esophagus (swallowing tube) or treatment area that causes swallowing difficulty and may require a feeding tube; this may last up to a year or may be permanent.
- Damage to the nerves that control the diaphragm, which could cause paralysis of the diaphragm and could be life threatening
- Hardening or thickening of the skin in the treatment area that causes swallowing difficulty and may require a feeding tube, which may be permanent
- Wounds that drain and/or won't heal and/or abnormal holes that connect two or more parts of the body, such as a hole between the windpipe and the swallowing tube; these can lead to infection, pain, or other problems that can be life threatening.
- Bleeding from the blood vessels that carry blood to the brain, which could cause a stroke or could be life threatening
- Serious damage to the jawbone or other bones in the head or neck that can lead to infection, bleeding, and/or pain; this sometimes requires surgery.
- Nerve damage within the head and neck that can cause weakness, numbness, or pain in the muscles of the face, neck, throat, arm(s), and/or hand(s); sometimes this damage can be permanent.

Risks Associated With Chemotherapy

Cisplatin

Likely

- Tiredness and/or general weakness
- Nausea and/or vomiting
- Decrease in white blood cell count, which may increase the risk of infection, decreased healing, and/or bleeding
- Decrease in red blood cell count, which may result in anemia, tiredness, and/or shortness of breath
- Decrease in platelets, the cells in the blood that help blood clot normally
- Loss of appetite and/or weight loss
- Ringing in the ears and/or hearing loss

Less Likely

- Decrease in the kidneys' ability to handle the body's waste, which may be permanent
- Changes in electrolytes, which may result in tiredness, cramps, and/or numbness and tingling
- Involuntary movements, restlessness, muscle cramps, and/or loss of coordination
- Numbness and tingling in the fingers, hands, toes, and feet
Rare
- Hair loss
- Loss of taste
- Changes in vision
- Seizures
- Loss of muscle or nerve function, which may result in weakness
- Allergic reactions, which can involve flushing, difficulty breathing, irregular heartbeat, low blood pressure, and can even be life threatening
- Another cancer called acute leukemia

5-FU (5-Fluorouracil)
Likely
- Decrease in white blood cell count, which may increase the risk of infection, decreased healing, and/or bleeding
- Decrease in red blood cell count, which may result in anemia, tiredness, and/or shortness of breath
- Loss of appetite
- Nausea and/or vomiting
- Diarrhea with cramping or bleeding
- Skin rash
- Fatigue
- Headaches
- Hair loss, which is temporary
- Mouth sores
- Sore throat

Less Likely
- Confusion
- Eye irritation, watering of eyes, and/or runny nose
- Redness, tenderness, peeling, and/or tingling of the palms and soles of feet
- Increased sensitivity to sunlight
- Darkening of the skin, nails, or veins
- Loss of coordination or balance

Less Likely, But Serious
- Damage to the heart or spasm of the heart’s blood vessels that can cause chest pain
- Inflammation of the liver, which may result in yellowing of skin and eyes, tiredness, and/or pain on upper right of the stomach area
- Infection at the catheter entry site
**Paclitaxel**

**Likely**
- Hair loss
- Tingling, numbness, burning pain in hands and feet
- Lower blood counts during treatment, which could lead to an increased risk of infection, weakness, and/or in bleeding and bruising easily
- Inflammation of the lining of the mouth
- Skin redness or rash

**Less Likely**
- Nausea and/or vomiting
- Diarrhea
- Changes in finger or toe nails
- Inflammation of the lining of the throat and/or intestines
- Tiredness
- Blurred vision and/or the feeling of seeing flashing lights
- Flushing
- Dizziness and/or lightheadedness
- Tenderness, hardness, or itching of the skin; rarely, blistering of the skin
- Pain in muscles and joints
- Changes in mood: being anxious or agitated

**Less Likely, But Serious**
- Reaction to paclitaxel, resulting in injury to the skin, lung, and/or lining of the digestive tract in the chest area that has received radiation
- Cardiovascular changes, such as low or high blood pressure, speeding up or slowing of heartbeat, a blockage of blood flow to the heart, and/or heart attack
- Seizures
- Allergic reactions, which could involve sweating, itching, hives, difficulty breathing, lightheadedness, and/or rapid heartbeat
- Severe inflammation of the small and large intestines
- Severe rash called Stevens-Johnson Syndrome, which can cause fever and red sores in your mouth and eyes
- Changes in liver enzymes in the blood, which may mean damage to the liver that could lead to being hospitalized, or rarely, to death

**Docetaxel**

**Likely**
- Decrease in white blood cell count, which may increase the risk of infection, decreased healing, and/or bleeding
- Decrease in red blood cell count, which may result in anemia, tiredness, and/or shortness of breath
- Tiredness and/or general weakness
- Unusual sleepiness
- Nausea and/or vomiting
- Mouth sores
- Diarrhea
- Loss of appetite, change in taste, and/or weight loss
- Loss of hair
- Headache
- Bloating and fluid retention in the hands, feet, and/or ankles
- Shortness of breath
- Muscle or joint pain
- Changes in the nails
- Inflammation of the eyes
- Numbness in fingers and in feeling

**Less Likely**
- Rash, redness and/or swelling of the skin
- Allergic reactions, which may involve rash, itching, fever, swelling, chills, or low back pain and which also can involve flushing, shortness of breath, and changes in blood pressure
- Inflammation of veins
- Irregular heartbeat
- Decrease in platelets, the cells in the blood that help blood clot normally
- Seizures
- Liver inflammation, which may result in yellowing of skin and eyes, tiredness, and/or pain on upper right of the stomach area
- Increased fluid around the lung and heart
- Swelling of feet

**Rare but serious**
- Lung inflammation, which may involve shortness of breath, cough, and/or fever
- Death

Chemotherapy drugs can decrease your white blood cells that fight infection. To help prevent infections, you will be given G-CSF, a drug to help your body make white blood cells.

**Risks Associated with G-CSF**

**Likely**
- Bone pain

**Less Likely**
- Headache
- Skin rash
- Fever
- Nausea and/or vomiting
- Loss of appetite and/or weight loss

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• Diarrhea or constipation
• Sore throat
• Swelling of feet due to increased fluid
• Speeding up or slowing of heartbeat
• Chest pain
• Low blood pressure
• Larger than normal spleen (the spleen makes blood cells); you may have pain in the upper abdomen
• Temporary mild swelling at injection sites

Reproductive Risks

Because the drugs in this study can affect an unborn baby, you should not become pregnant or father a baby while on this study. Pregnant women are excluded from participation in this study. Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are considered to be: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), Depo Provera, Norplant, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable method involves the careful use of condoms and a spermicidal foam or gel and/or a cervical cap or sponge. You should not nurse a baby while on this study. If you become pregnant while taking part in this research study, tell one of the study doctors immediately. We encourage you to ask your doctor about counseling and more information about preventing pregnancy.

If you are a man able to father children, the treatment you receive may risk harm to an unborn child unless you use a form of birth control approved by your doctor. If you are unwilling to use adequate birth control measures while on treatment and for at least three months thereafter to prevent pregnancy, you should not participate in this study. If you suspect you have caused anyone to become pregnant, you must tell your doctor immediately.

BENEFITS

Taking part in this study may or may not make your health better. While doctors hope that a combination of re-irradiation and chemotherapy will result in better control of your head and neck cancer compared to chemotherapy alone, there is no proof of this yet. We do know that the information from this study will help doctors learn more about re-irradiation and chemotherapy as treatments for cancer. This information could help future cancer participants.

ALTERNATIVES

You may choose to not participate in this study. Your other choices may include:
• Getting treatment or care for your cancer without being in a study
• Taking part in another study
• Getting no treatment
• Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Your doctor can tell you more about your condition and the possible benefits of the different available treatments.

The physicians involved in your care will be available to answer any questions you have concerning this program. In addition, you are free to ask your physician(s) any questions concerning this program that arise in the future.

CONFIDENTIALITY
Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Records of your progress while on the study will be kept in a confidential form at this institution and in a computer file at the headquarters of the Radiation Therapy Oncology Group (RTOG). A group of experts in head and neck cancer from the RTOG Head & Neck Committee, the study chairs, and the RTOG study statistician will be reviewing the data from this research periodically throughout the study. Your personal information may be disclosed if required by law. Also your records may be reviewed by the UAB Institutional Review Board (IRB), The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people. The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide participants and doctors greater access to cancer trials.

If you receive services in University Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at this facility.

WITHDRAWAL WITHOUT PREJUDICE
Taking part in this study is voluntary. You are free to withdraw your consent and to discontinue participation in this study at any time without prejudice against further care that you may receive at this institution. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

SIGNIFICANT NEW FINDINGS
Significant new findings that develop during the course of the research that may relate to your willingness to continue your participation in this study will be provided to you.
COSTS FOR PARTICIPATION IN THE STUDY
You or your insurance company will be charged for standard medical care and/or hospitalization for the treatment of your cancer. If the routine costs are billed to Medicare, it will be noted on the claim that the services were provided in a clinical trial. Information relating to this study, including your name, medical record number, date of birth and social security number may be shared with the billing offices of UAB and UAB Health System-affiliated entities so that claims may be appropriately submitted to the study sponsor or to your insurance company for clinical services and procedures provided to you during the course of this study.

PAYMENT FOR PARTICIPATION IN RESEARCH
You will receive no payment for taking part in this study.

PAYMENT FOR RESEARCH RELATED INJURIES
UAB, the Radiation Therapy Oncology Group, and the National Institutes of Health have made no provision for monetary compensation in the event of injury resulting from the research, and in the event of such injury, treatment is provided but is not provided free of charge.

QUESTIONS

For more information about clinical trials:

You may call the NCI’s Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

Visit the NCI’s Web sites: Cancer Trials: comprehensive clinical trials information http://cancertrials.nci.nih.gov


For more information concerning any of the procedures, you may contact Lisa Clemons, R.N. at (205) 975-2880 or Susan Suter, R.N. at (205) 975-0868.

If you have any questions about the research or a research-related injury, you may contact the principal investigator, Dr. Ruby Meredith at (205) 934-2760.

If you have any questions about policies, the conduct of the study, or the rights of research subjects, you may contact Ms. Sheila Moore, Director of the Office of the Institutional Review Board for Human Use (IRB). Ms. Moore can be reached at (205) 934-3789 or 1-800-822-8816, press the option for an operator/attendant and ask for extension 4-3789 between the hours of 8:00 a.m. and 5:00 p.m. CT, Monday through Friday.
LEGAL RIGHTS

You are not waiving any of your legal rights by signing this form.

SIGNATURES

Your signature below indicates that you agree to participate in this study. Your signature indicates that you have read (or been read) the information provided above. You will receive a signed copy of this informed consent.

______________________________  ________________________
Signature of Participant        Date
 or Legally Authorized Representative

______________________________  ________________________
Signature of Investigator       Date

______________________________  ________________________
Signature of Witness            Date

______________________________  ________________________
Signature of Person Obtaining Consent
(If other than investigator)    Date
What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your health information may be used for the research.

Participant name: ___________________________ UAB IRB Protocol Number: F050712004
Research Protocol: RTOG 0421 - A Phase III Trial for Locally Recurrent, Previously Irradiated Head and Neck Cancer: Concurrent Re-Irradiation and Chemotherapy Versus Chemotherapy Alone
Principal Investigator: Ruby F. Meredith, MD, PhD
Sponsor: Radiation Therapy Oncology Group

What health information do the researchers want to use? All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.

Why do the researchers want my health information? The researchers want to use your health information as part of the research protocol listed above and described to you in the Informed Consent document.

Who will disclose, use and/or receive my health information? The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, The Children’s Hospital of Alabama, Callahan Eye Foundation Hospital and the Jefferson County Department of Public Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; and outside regulatory agencies, such as the Food and Drug Administration.

How will my health information be protected once it is given to others? Your health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel the Authorization? You may cancel this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the health information that was provided before you cancelled your authorization.

Can I see my health information? You have a right to request to see your health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: ___________________________ Date: __________
or participants’ legally authorized representative: ___________________________ Date: __________
Printed Name of participant’s representative: ___________________________
Relationship to the participant: ___________________________

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